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## **REMARKS**

### **I. Amendments**

By this amendment, claims 1, 4, 7, 11, 23 and 25 have been amended, claims 2 and 3 have been cancelled and new claims 28-49 have been added.

This amendment adds no new matter to the specification. Support for this amendment is found in the specification and claims as filed.

Specifically, the new claims recite methods of treating mammals with a combination of insulin sensitizer and anorectic.

No amendment of inventorship is necessitated by this amendment.

### **II. Discussion of the Rejection under 35 U.S.C. Sec. 112, First Paragraph**

Claims 1-7, 11 and 22-27 have been rejected under 35 U.S.C. Sec. 112, first paragraph, as allegedly non-enabled with respect to the recited method.

Applicants respectfully disagree that their invention, as set forth in the pending claims as amended, is not enabled. As previously indicated, Applicants have provided a working example: Example 1, starting on page 34 of the specification. The Examiner's position is that this example only enables the method claims for pioglitazone and mazindol, and only at a specific dosage.

By this amendment, Applicants have limited the insulin sensitizers in the method of claim 1 to those falling under general formula (I). Moreover, in the specification, the ranges for the appropriate dosages are described on page 28, line 16- page 29, line 14; appropriate anorectics are described on page 20, lines 17-36 and the insulin sensitizers are described on page 6, line 3 – page 18, line 5. Applicants believe that independent method claim 1 is fully enabled, given the working example and the teachings of the specification.

The Examiner has not provided an adequate reason why one skilled the art could not use the presently claimed method for the recited insulin sensitizer genus and anorectics without undue experimentation. Accordingly, Applicants believe that the aspect of their invention, as set forth in independent method claim 1 is adequately enabled.

Claims 2 and 3 have been cancelled. Claims 4-7, 11 and 22-24, 26 and 27 depend upon claim 1. Applicants assert that the more specific dependent claims are also adequately enabled for the same reason.

Moreover, claim 7 is already limited to the specific insulin sensitizer and specific anorectic which the Examiner has decided are enabled by virtue of the working example. By this amendment, claim 7 has been made an independent claim.

By this amendment, claim 25 has also been made independent.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, first paragraph rejection.

### **III. Discussion of the Rejection of Claim 23 under 35 U.S.C. Sec. 112, First Paragraph**

Claim 23 has been rejected under 35 U.S.C. Sec. 112, first paragraph, as allegedly non-enabled with respect to various analogues of anorectics.

By this amendment, claim 23 has been amended to delete the analogues.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, first paragraph rejection of claim 23.

### **IV. Discussion of the Rejection of Claims 3 and 11 under 35 U.S.C. Sec. 112, Second Paragraph**

Claims 3 and 11 have been rejected under 35 U.S.C. Sec. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

By this amendment, claim 3 has been cancelled.

Also by this amendment, claim 2 has been cancelled. Due to these changes, the rejection is moot.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, second paragraph rejection of claims 3 and 11.

**V. Discussion of the Rejection under 35 U.S.C. Sec. 103(a) over Ikeda *et al.* in view of El-Din *et al.* and Sundrehagen**

Claims 1-7, 11, 22, 26 and 27 have been rejected under 35 U.S.C. Sec. 103(a) as allegedly being unpatentable over Ikeda *et al.* (EP 0 749 751); El-Din *et al.* (Egypt J. Pharm. Sci. article, 1988) and Sundrehagen (WO 90/13818). Applicants respectfully traverse the rejection.

By this amendment, claim 1 has been amended to recite the insulin sensitizers of general formula (I). This amendment adds no new matter to the specification, as it merely incorporates the subject matter of original claim 2. Due to the change of claim 1, claim 2 has been cancelled.

Applicants do not believe that the combined teachings of the cited references render their invention as set forth in the pending claims obvious, and they do not even believe that it would be appropriate to combine the cited references, as will be explained below.

The Examiner has cited the El-Din *et al.* reference for its disclosure of the anorectic mazindol. Yet, the El-Din *et al.* reference recites treating diabetic rats with an oral hypoglycemic drug (tolbutamide) and an anorexigenic drug (fenfluramine or mazindol); and proves that co-treatment with mazindol did not provide a desirable result, as mazindol failed to potentiate the effect of tolbutamide. Moreover, the combination of tolbutamide and fenfluramine even caused hyperglycemia. How the Examiner can utilize this reference to show that their invention is obvious is difficult for Applicants to understand, as if anything, the reference teaches away from combinations including mazindol. To utilize the reference only for its citation of mazindol ignores the scientific basis for the article.

The deficiencies of El-Din *et al.* are not cured by Ikeda *et al.* Ikeda *et al.* is cited by the Examiner for its teaching of insulin sensitizers.

The teachings of Sundrehagen does not cure the deficiencies of the Ikeda *et al.* and El-Din *et al.* references. Sundrehagen is directed to a method of assaying glycosylated hemoglobin, which is useful for the *in vitro* diagnosis and monitoring of diabetes mellitus.

Applicants disagree that one skilled in the art could utilize the teachings of Sundrehagen to be motivated to combine the insulin sensitizers of Ikeda *et al.* with the anorectic of El-Din *et al.* to obtain their invention as set forth in claim 1 as amended. Sundrehagen teaches how to monitor glycosylated hemoglobin; but not what will lower glycosylated hemoglobin in the body. Merely because each individual component may be effective would not be sufficient motivation to combine the teachings of El-Din *et al.* and Ikeda *et al.*, especially since El-Din *et al.* teach that

combination with mazindol is *ineffective*. This is contrary to the Examiner's assumption that the teachings of the three references can be combined. Therefore Applicants do not believe that their invention as set forth in independent method claim 1 as amended is rendered obvious by the cited art.

Claims 2 and 3 have been cancelled. Claims 4-6, 11, 22, 26 and 27 depend upon claim 1. Claim 7 has been made independent. Applicants assert that these more specific claims are also patentable over the combined teachings of the cited references for the same reason.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 103(a) rejection.

#### **VI. Discussion of the Rejection under 35 U.S.C. Sec. 103(a) over Ikeda *et al.* in view of Heath *et al.* and Sundrehagen**

Claims 1-5, 11, 22, 24, 26 and 27 have been rejected under 35 U.S.C. Sec. 103(a) as allegedly being unpatentable over Ikeda *et al.* (EP 0 749 751); Heath *et al.* (Diabetes article, 1999) and Sundrehagen (WO 90/13818). Applicants respectfully traverse the rejection.

As an initial matter, Applicants assert that the Heath *et al.* article is not proper art, as their Japanese priority application was filed June 30, 1998; and the article was not published until 1999.

The deficiencies of Heath *et al.* are not cured by Ikeda *et al.* Ikeda *et al.* is cited by the Examiner for its teaching of insulin sensitizers. The present invention as set forth in independent claim 1 as amended is directed to a method for lowering the concentration of glycosylated hemoglobin with a combination of an insulin sensitizer and an anorectic. There is no teaching or suggestion for combining the insulin sensitizers of the cited reference with anorectics as in the claimed method.

On page 8, lines 34-37, examples of drugs which can be combined with insulin sensitivity enhancers are listed. Anorectics are not among them.

The teachings of Sundrehagen do not cure the deficiencies of the Ikeda *et al.* reference, as Sundrehagen teaches a method of assessing glycosylated hemoglobin in a sample, and not what compounds may be useful for lowering glycosylated hemoglobin.

Claims 2 and 3 have been cancelled. Claims 4-5, 11, 22, 24, 26 and 27 depend upon claim 1. Applicants assert that the more specific dependent claims are also patentable over the combined teachings of the cited references for the same reason.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 103(a) rejection.

**VII. Discussion of the Rejection of Claim 23 under 35 U.S.C. Sec. 103(a) over Ikeda *et al.* in view of Heath *et al.* and Sundrehagen and Holst *et al.***

Claim 23 has been rejected under 35 U.S.C. Sec. 103(a) as allegedly being unpatentable over Ikeda *et al.* (EP 0 749 751); Heath *et al.* (Diabetes article, 1999); Sundrehagen (WO 90/13818) and Holst *et al.* (WO/97/31943). Applicants respectfully traverse the rejection.

As an initial matter, Applicants assert that the Heath *et al.* article is not proper art, as their Japanese priority application was filed June 30, 1998; and the article was not published until 1999.

The deficiencies of Heath *et al.* are not cured by Ikeda *et al.* Ikeda *et al.* is cited by the Examiner for its teaching of insulin sensitizers. The present invention as set forth in independent claim 1 as amended is directed to a method for lowering the concentration of glycosylated hemoglobin with a combination of an insulin sensitizer and an anorectic. Claim 23 depends upon this independent claim, and recites certain anorectics. There is no teaching or suggestion for combining the insulin sensitizers of the cited reference with anorectics as in the claimed method.

On page 8, lines 34-37, examples of drugs which can be combined with insulin sensitivity enhancers are listed. Anorectics are not among them.

The teachings of Sundrehagen do not cure the deficiencies of the Ikeda *et al.* reference as Sundrehagen teaches a method of assessing glycosylated hemoglobin in a sample, and not what compounds may be useful for lowering glycosylated hemoglobin does not appear to refer to anorectics; and moreover the teachings of Holst *et al.* do not cure the deficiencies of Sundrehagen and Ikeda *et al.* Holst *et al.* is recited by the Examiner as merely teaching certain specific compounds.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 103(a) rejection.

## VIII. Discussion of the Rejection for Obviousness-Type Double Patenting

Claims 1-7, 11 and 22-27 have been rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 13-25 of U.S. Patent No. 6,329,404.

The '404 patent is in the same family as EP 0 749 751, the Ikeda *et al.* reference. As this reference does not disclose the anorectics recited in the claims or a method of lowering the concentration of glycosylated hemoglobin as stated by the Examiner on pages 4-5 of the Office Action, Applicants do not believe there is any double-patenting issue.

Furthermore, Applicants do not believe that the teachings of Sundrehagen (a method of assessing glycosylated hemoglobin in a sample; which does not indicate what compounds may be useful for lowering glycosylated hemoglobin, and furthermore does not appear to refer to anorectics) can be used to contribute to a double-patenting rejection in this instance.

Therefore, Applicants respectfully request withdrawal of the rejection for obviousness-type double patenting.

## IX. Conclusion

Reconsideration of the claims and allowance is requested.

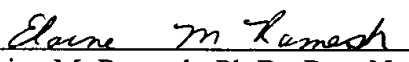
Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, she is respectfully requested to call Applicants' attorney at (847) 383-3391.

Respectfully submitted,

Dated: December 18, 2003

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